REMARKS

The Present Invention

The present invention pertains to citalopram hydrobromide with specific crystal properties and a method of crystallizing citalopram hydrobromide.

The Pending Claims

Claims 21-37 are currently pending. Reconsideration of the pending claims is respectfully requested.

Amendments to the Claims

The claims have been amended to more particularly point out and distinctly claim the present invention. In particular, claims 1-9 and 12-20 have been canceled. Claims 10 and 11 had been canceled previously. Claims 21-27 have been added and are supported by originally filed claims 1, 2, and 4-6 and the specification at, for example, page 2, line 25, through page 3, line 4. Claims 28-37 are the same as previously pending claims 9 and 12-20 but have been reordered for ease of reference. In that respect, therefore, claims 28-30 and 32-37 are supported by originally filed claims 9 and 12-19, and claim 31 is supported by the specification at, for example, page 9, lines 21-29. No new matter has been added by way of these amendments.

Summary of the Office Action

Claims 1-9 and 12-20 are rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent 4,650,884 (Bogeso).

Discussion of the Obviousness Rejection

According to the Office Action, the Examiner contends that Bogeso discloses the inventive method and only differs by not mentioning that the cooling rate should be controlled. The Examiner also concedes that Bogeso does not disclose the particle size or the aspect ratio of the citalopram hydrobromide crystals. According to the Examiner, applicants must show the beneficial effect of controlling the cooling rate on the size of the citalopram crystals compared to the crystals obtained by Bogeso. In addition, the Examiner states that applicants also must demonstrate that the crystals obtained by the claimed method have superior properties and/or benefits compared to citalopram crystals previously prepared in the art.

Claims 1-9 and 12-20 have been canceled, and the rejection of these claims is moot. However, new claims 21-37 are based on claims 1-9 and 12-20, and applicants traverse the rejection to the extent it is applicable to the new claims for the following reasons.

The present invention, as defined by pending claims 21-37, pertains to citalopram hydrobromide crystals having an average aspect ratio of not less than 2.0 and not more than 9.0 (claims 21-27) and a production method of citalopram hydrobromide crystals (claims 28-37). The claimed citalopram hydrobromide crystals can improve production problems "such as poor filtering performance after crystallization for the preparation of a pharmaceutical bulk and poor fluidity when crystals are being taken out" (see the specification at, for example, page 12, line 32, through page 13, line 3). In other words, the present inventive crystals with the claimed aspect ratio have simultaneously solved the problems of filtering performance and fluidity.

In contrast, as conceded by the Examiner, Bogeso does not describe the aspect ratio of the obtained citalopram hydrobromide crystals. Moreover, Bogeso does not teach or suggest that a citalopram hydrobromide crystal such as that of the present invention can solve the aforementioned production problems. Specifically, Bogeso discloses the recrystallization of citalopram hydrobromide from the following solvents:

1st recrystallization: water
2nd recrystallization: methanol/2-propanol
3rd recrystallization: methanol/acetone/hexane

For the first and second recrystallizations, the solution is cooled to 20 °C and left overnight for crystallization (col. 5, lines 35-44). As for the third recrystallization, Bogeso discloses that hexane is slowly added after the solution is cooled to 20 °C and seed crystals are added (col. 5, lines 48-53). Based on this information, it is believed that crystals start to precipitate out of solution only after being cooled to 20 °C in any of the three recrystallization steps. This belief is based on a similar step in Comparative Example 1 of the instant application.

In Comparative Example 1, citalopram hydrobromide crystals precipitated out of solution only after cooling the solution to 20 °C and the addition of a seed crystal (page 18, lines 12-37). As shown in the micrograph of the crystals obtained in Comparative Example 1 (see Figure 16), the aspect ratio of the resulting citalopram hydrobromide crystals is approximately 1. Since the average aspect ratio of a crystal relates to its overall shape and is measured as the ratio of the length of the crystal to its width, a crystal with an average aspect ratio of 1 (i.e., 1:1) is perfectly spherical. Since Bogeso teaches a similar method, the crystals obtained by the recited method of Bogeso also would be reasonably expected to have an

aspect ratio of approximately 1. See, also, the specification at page 1, line 17, through page 2, line 4. As such, Bogeso does not teach or suggest preparing a citalopram hydrobromide crystal with an average aspect ratio of not less than 2.0 and not more than 9.0.

Regarding method claims 28-37, as conceded by the Examiner, Bogeso does not disclose cooling the citalopram hydrobromide to allow for crystallization while controlling the cooling rate. Controlling the cooling rate is imperative in obtaining citalopram hydrobromide crystals of the present invention.

As explained above, Bogeso does not teach or suggest an average aspect ratio of not less than 2.0 and not more than 9.0 nor controlling the cooling rate of crystallization. Moreover, Bogeso does not appreciate any benefits of providing a citalopram hydrobromide crystal with an average aspect ratio of not less than 2.0 and not more than 9.0. Accordingly, one of ordinary skill in the art would not be motivated, nor know how, to alter the disclosure of Bogeso in such a way so as to arrive at the invention of claims 21-37.

As such, it cannot be said that the present invention is obvious in view of Bogeso, and applicants request that the rejection be withdrawn.

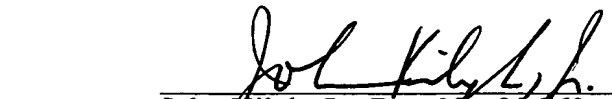
Information Disclosure Statement

An Information Disclosure Statement is filed concurrently herewith to identify a reference which was filed on May 8, 2004 as a third party observation against the European counterpart of the present patent application. The Examiner is requested to confirm consideration of the reference by appropriately initialing and returning to applicants a copy of the PTO Form-1449 that accompanies the Information Disclosure Statement.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



John Kilyk, Jr., Reg. No. 30,763
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

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